MEDPAGE TODAY®

Meeting Coverage > AASLD

Novel Tx for Hepatic Encephalopathy Works Fast

— Lowers ammonia level more quickly than standard care, study finds

by Joyce Frieden, News Editor, MedPage Today

October 22, 2017

This article is a collaboration between MedPage Today® and:

WASHINGTON -- A new treatment for hepatic encephalopathy worked faster than usual care to reduce patients' ammonia levels, researchers said here.

In patients diagnosed with confirmed hyperammonemia at baseline, the new treatment, ornithine phenylacetate (OCR-002), lowered ammonia levels faster and led to faster clinical improvement compared with placebo, with a 21-hour median reduction in time to improvement (*P*=0.034), reported Robert Rahimi, MD, of the Baylor University Medical Center in Dallas, and colleagues in a poster presentation at at the Liver Meeting, the annual conference of the American Association for the Study of Liver Diseases.

OCR-002 "effectively binds ammonia, which we think is one of the very important curative mechanisms in hepatic encephalopathy," Stanley Bukofzer, MD, study co-author and chief medical officer at Ocera Therapeutics, which sponsored the trial, told *MedPage Today* in an interview. "If you can reduce the ammonia exposure in these patients, you can save the patients, get them over whatever caused the acute exacerbation ... and get them out of the hospital and back into some more normal functioning."

Time is of the essence in this disorder, he added. "The longer you leave [this problem], the more risk these patients are at ... You want to treat the patients as early and quickly as possible, and [OCR-002] seems to get the ammonia down very quickly."

Hepatic encephalopathy is a serious complication of cirrhosis, accounting for about 400,000 hospital admissions each year. Overall, about 15% of patients who experience this event will die from it, "so it's a very high-risk group of patients," Bukofzer said.

this stroke will die from it," so it's a very high-risk group of patients," Bajaj said. Although rifaximin is commonly used for prophylaxis, it is not indicated for acute encephalopathy in hospitalized patients.

The researchers wanted to know whether OCR-002, which uses a novel scavenger mechanism to lower ammonia levels, would be helpful in these patients. They randomized 231 patients with cirrhosis and an acute episode of hepatic encephalopathy stages 2, 3, or 4 to either OCR-002 or placebo. The dose of the drug -- determined by the degree of liver failure -- was either 10, 15, or 20 g, infused intravenously daily for 5 days.

The treatment groups were comparable in baseline characteristics, with the majority in each group being male (62% of patients receiving the intervention and 68% of those on placebo) and members of each group at similar Child-Pugh stages. The mean age was 59 in the OCR-002 group and 60 in the placebo group.

As for inciting factors, bacterial infection was the most common (found in 29 of the 231 patients in the study), followed by poor compliance (28 patients), dehydration (25 patients), and presence of a transjugular intrahepatic portosystemic shunt (16 patients).

A total of 59 patients in the placebo group completed the 5-day treatment, as did 116 of the treatment group. Reasons for discontinuation included early discharge from the hospital, decision by the investigator, or an adverse event.

The most common adverse events included hypokalemia, pyrexia, urinary tract infection, and anemia. Serious adverse events occurred in 25% of the treatment group and 29% on placebo; mortality rates during the study were 9% in the treatment group and 13% in the placebo group.

Although the primary endpoint of median time to improvement in the intent-to-treat population wasn't statistically significant, the response rate -- defined as time to clinical improvement at 48 hours -- was significantly higher with the study drug than with placebo (P=0.028). In addition, patients on the study drug were discharged from the ICU about 1.5 days earlier, although this finding was not statistically significant.

This work is very important "because for the first time this substance was tested in a very good quality study," said Arnulf Ferlitsch, MD, a hepatologist at the Medical University of Vienna in Austria, who was not involved in the study. "This was always the problem with L-ornithine L-aspartate [a drug with a similar mechanism], that the data are lacking."

Drugs like these are especially needed because hepatic encephalopathy "is a problem which about a third of patients with cirrhosis will have to face, so treating this disease and preventing recurrence is a very important [issue]," Ferlitsch said. "In particular, "it would be a big help for us if we had the substance in oral form for use prophylactically at

would be a big help for us if we had the substance in oral form for use prophylactically at home by patients."

Rahini reported relevant relationships with Ocera Therapeutics. Bukofzer had no disclosures.

- This activity is part of our Clinical Context curriculum in Hepatitis C

Primary Source

American Association for the Study of Liver Diseases

Source Reference: *Rahimi RS, et al "STOP-HE: A Randomized, Double-blind, Placebo-controlled Study of OCR-002 in Patients with Hepatic Encephalopathy" AASLD 2017; Abstract 502.*